Phase Behavior of (Polyacrylamides + Water) Solutions. Concentration, Pressure and Isotope Effects

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Keywords: data, liquid-liquid equilibria, polyacrylamides, polymeric aqueous solutions, pressure effects, isotope effects.

ABSTRACT

Phase diagrams of PIPAM as well as of hydrophylically-modified copolymers in aqueous solution have been determined. A high-accuracy He-Ne *LASER* scattering technique has been used for the detection of operational spinodal and cloud-point curves. Polymer concentrations have varied from 0.5 to 20 weight percent. In the case of copoly (PIPAM/vinylsaccharide) several different chain lengths have been considered. Pressure (up to 400 bar) and solvent isotope effects have been studied. We predict a closed-loop type phase diagram for the copolymers, which presents an estimated hypercritical point in H_2O solutions at $M_W \sim 0.5 \times 10^5$, although only LCST´s are experimentally accessible. At lower molecular weights, the solutions are always in the one-phase region.

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INTRODUCTION

Poly(N-isopropylacrylamide), the so-called PNIPAAM, or simply PIPAM, is fairly soluble in water at room temperature and atmospheric pressure. Interest from the scientific and industrial community in PIPAM, has been growing, especially in the last decade, since it has a large number of potential applications, including immobilization of enzymes and protein separation [1,2]. It has probably become the most popular member of a class of polymers that possesses inverse solubility in aqueous solutions upon heating, a property which it shares with some other polymers capable of interacting through hydrogen-bonds with water, but contrary to the behavior of most polymers in solution. Despite current interest in PIPAM, accurate data concerning its phase equilibria in water [1-5] are still scarce, hence this work.

The degree of solubility and the (p,T,x) conditions of its occurrence is a consequence of the interplay between hydrophilic and hydrophobic forces in solution, and experimentally observed phase transition occurs at the so-called Lower Critical Solution Temperature (LCST) curve. An easy way of controlling the hydrophilic/hydrophobic balance is to add sugars in distinct proportions. This can be done either in the solution (where the sugar competes with the polymer for dissolution) or in the polymer (copolymerization), or in both. In this work, we have therefore chosen to study a copolymer [6] as well as PIPAM, representing thus, a pseudo-ternary mixture with about 13-14 mol percent of a vinylsaccharide (VS) highly hydrophilic, 1-deoxy-1- methacrylamido-D-glucitol, in PIPAM, plus water.

The experimental technique for the detection of phase transitions uses the increase of scattered light and the simultaneous decrease of the transmitted one that results from

shining the sample with a He-Ne LASER beam as the solution undergoes phase separation [7].

Different polymer concentrations and molecular weights have been used. Pressure ranges from atmospheric up to 400 bar. With the aim of achieving a better understanding of the nature of the equilibrium involved, the solvent isotope effect in the phase diagrams of the polymer solutions has also been investigated.

EXPERIMENTAL

Polymer synthesis and characterization

The homopolymer poly(N-isopropylacrylamide) (PNIPAAM) and several copolymers with a vinyl saccharide monomer, more precisely copoly(N-isopropylacrylamide/1-deoxy-1-methacrylamide-D-glucitol), have been synthesized by radical polymerization.

The reactions were carried out in 5 cm^3 magnetically stirred microvials, under nitrogen atmosphere at 25ºC in an aqueous solution during 24 h, using the redox pair $(NH_4)_2S_2O_8/Na_2S_2O_5$ as a radical initiator. The concentration relationship between the oxidative part of the redox couple ($(NH_4)_2S_2O_8$, concentration $2.0x10^{-2}$ M) and the reductive part ($Na_2S_2O_5$, concentration $7.5x10^{-2}$ M) was maintained constant in all experiments. These concentrations correspond to the values reported in the literature as giving rise to the highest yield on the homopolymerization reaction of 1-deoxy-1-methacrylamido-D-glucitol [6].

In order to obtain products with different average molecular weights, copolymerizations were performed using an initial comonomer composition of 10 mol percent of vinyl saccharide (VS), and different amounts of radical initiatior, namely 0.2%,

1.0%, 1.5% and 2.0% (mol percent on monomers). Polymers were purified by ultrafiltration and recovered by freeze-drying.

The vinyl saccharide monomer was previously synthesized according to the literature [6], by reacting 1-amino-1-desoxy-D-sorbitol (*Aldrich Chem. Co*.) with methacrylic anhydride (*Fluka*). In the homopolymerisation reaction of N-isopropylacrylamide (*Aldrich Chem. Co*.) 0.6 mol percent of monomer of radical initiator was used.

The copolymer composition was determined by elemental analysis of C, H and N. Capillary viscometry in 0.1M Na_2SO_4 solution at 25ºC was performed to determining the viscosity limit number. Using static multi-angle *laser* light scattering (*Dawn DSP Laser Photometer*) all copolymers have been characterized to obtain the weight average molecular weight, $\overline{M}_W$. Polydispersities, $\overline{M}_W / \overline{M}_n$, have been measured by GPC/SEC in a *Waters* apparatus at 25ºC using water as eluent and a *Waters Hydrogel Linear* column. Using monodisperse pullulan standards (*Shodex*, in the molecular weight range 0.59×10^4 to 78.8×10^4) the calibration curve has been generated. The characteristics of polymer samples used in this work are reported in Table 1.

Sample	Polymer	VS content (mol %)	$[\eta]$ $(ml.g^{-1})$	$\overline{M}_W$ $\times 10^{-5}$	$\overline{M}_W / \overline{M}_n$
P1	PNIPAAM	-	62.7	6.15	4.4
CP1	Copoly(PNIPAAM/VS)	14.0	56.1	4.32	4.0
CP2	Copoly(PNIPAAM/VS)	12.9	16.2	1.70	2.1
CP3	Copoly(PNIPAAM/VS)	13.7	1.02	1.10	2.0
CP4	Copoly(PNIPAAM/VS)	13.3	0.38	0.56	2.0

Table 1. Polymer characteristics.

Solvents

H$_2$O used in this work was doubly distilled and deionized (*Millipore* equipment) and stored in sealed microvials. D$_2$O was purchased from *Aldrich Chem. Co.* with a claimed purity of 99.9 atom % D, and used as received. In order to avoid background turbidity, in all cases and prior to the injection into the light scattering cells, solutions were filtered from suspended impurities.

Equipment and Technique

The He-Ne *LASER* light scattering apparatus as well as the methodology used for the detection of phase transitions have very recently been described in great detail [7]. In the case of experiments where pressure was raised above 50 bar, a sapphire/stainless steel cell replaced the original glass capillary cell. In this case, the hydraulic fluid is the pure solvent (in this work, water) contacting a sufficiently long (1/16)´´ SS tubing filled with the solution, in order to avoid contamination during compression/expansion cycles. Cloud-point temperature accuracy is typically ±0.01 K in the range $240 < T/K < 400$, decreasing to ±1K in the case of spinodals, which are obtained from a large extrapolation [7,8] to the point where the inverse of the scattered light intensity reaches a null value. As for pressure, accuracy is ±0.1 bar up to 50 bar, decreasing to ±1bar in the range $50 < p/bar < 600$. Solutions were made up gravimetrically, and left stirring for several hours (sometimes for several days) in sealed vials before being injected to the measuring cell.

RESULTS AND DISCUSSION

Phase diagrams of polymer solutions are usually represented as two-dimensional cross-sections of a multi-dimensional space that embraces variables such as temperature, pressure, composition, polymer molecular weight, polymer polydispersity, and isotopic label either in the solvent, or in the polymer, or in both [8,9]. In this work, we have studied five distinct polymeric systems (see Table 1) in H_2O and/or in D_2O.

System (PIPAM + H$_2$O)

The effects of pressure and polymer composition (expressed as polymer weight percent, $\%W_p$) on both the cloud-point (cp) and material spinodal (sp) temperatures (T_{cp} and T_{sp}, respectively) are reported in Table 2 for [PIPAM ($\overline{M}_W = 615,500$) + water].

Wp	p/MPa	T_{cp}/K	T_{sp}/K	Wp	p/MPa	T_{cp}/K	T_{sp}/K
				4.167	30.0	308.27	
1.030	0.10	307.20					
2.011	0.10	306.74	321.6	4.167	40.0	308.32	
2.502	0.10	306.65		4.529	0.10	306.32	310.7
3.574	0.10	306.46	312.1	5.646	0.10	306.10	308.9
3.701	0.10	305.59		6.402	0.10	306.25	307.8
4.167	0.10	305.50	309.2	6.774	0.10	306.40	308.7
4.167	1.00	305.60	308.5	7.670	0.10	306.35	309.1
4.167	2.50	305.70	309.0	8.839	0.10	306.46	308.7
4.167	3.00	305.73	308.2	10.57	0.10	305.89	
4.167	4.00	305.86	307.6	11.46	0.10	306.20	309.1
4.167	5.00	305.90	307.4	14.74	0.10	305.84	308.7
4.167	20.0	308.12		17.57	0.10	305.72	310.9

Table 2. Cloud-point temperatures, T_{cp}, and spinodal temperatures, T_{sp}, at distinct polymer weight percentage, W_p, and pressure, p, for sample P1 (see Table 1 and text).

Isobars of cloud-points were obtained from the value of temperature where the intensity of transmitted light and scattered light suffer a sudden decrease and increase, respectively.
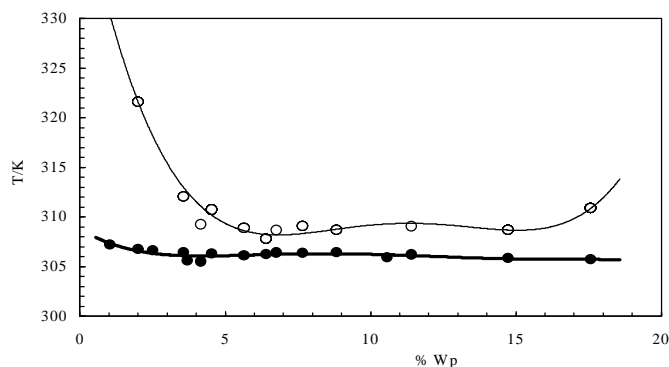

Figure 1: Cloud-point and spinodal temperatures *vs*. polymer composition (in weight percent) for PIPAM+H_2O (see Table 1) at a nominal pressure of 0.1 Mpa. Thick line and (●) represent experimental *cp* curve and individual *cp* temperatures, respectively. Thin line and (○) represent *sp* curve and individual *sp* temperatures, respectively.

Figure 1 depicts the T (%Wp) phase diagram at a nominal pressure of 0.1 Mpa, while Figure 2 represents the pressure dependence of cloud-point temperatures at a nominal composition $Wp = 4$ %.
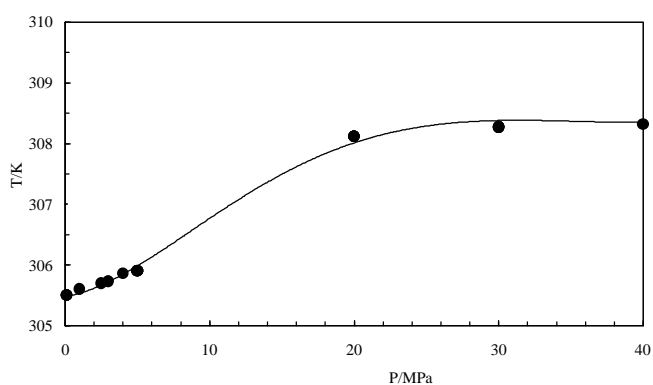

Figure 2: Pressure effects on the cloud-point temperature of a nominal 4 % solution of (PIPAM+H_2O). Quantitative similar curves have been observed for higher and lower concentrations.

It should be emphasized that while the composition dependence of *cp* temperatures is fairly small in the range 0-20 %, in contrast, *sp* temperatures show a significant composition dependence. At temperatures lower than *cp* the system is in the one-phase homogeneous region. At temperatures between *cp* and *sp* the system is materially metastable in respect to phase separation, and formation of the second phase should occur by a nucleation-and-growth mechanism. Finally, at temperatures above the *sp* curve, the system is materially unstable and phase separation should occur by the so-called spinodal decomposition. In summary, one can state that under stable equilibrium conditions precipitation of the polymer-rich phase upon heating is almost independent of polymer concentration, but if one is able to avoid stable equilibrium separation by diving into the metastable region, then, polymer concentration should be taken into consideration. For (highly) polydisperse systems, the liquid-liquid critical point does not necessarily coincide with the minimum of the LCST curve, but more precisely with the point of tangency between the *cp* and *sp* curves [9]. Analysis of our data indicate that the composition of the critical point at nominal 0.1 Mpa is $Wp_c = 6.5 \pm 0.5$ %. It is interesting to note that while cloud-point temperatures increase as pressure increases (see Figure 2), the opposite is observed for spinodal temperatures (Table 2). Since this comparison is being made at 4% (a value which is slightly smaller than that corresponding to critical composition), this unusual behavior seems to be an indication that critical composition is moving to lower values upon pressurization. It should also be noted that the slope of the temperature-pressure curve of phase separation (Figure 2) decreases to zero as pressure increases to 400 bar. Using thermodynamic arguments it can be shown [10] that regions of the phase diagram where the

temperature of phase separation is pressure independent correspond to ideal mixing (null value for the excess volume, v^E). On the other hand, for a LCST type of phase separation, a positive slope - as that observed in the major portion of Figure 2 – implies contraction ($v^E <$ 0) upon mixing, which favors miscibility as pressure is increasing.

Due to the fact that synthesis and characterization of PIPAM are difficult and tedious, and, above all, since other authors [3,5] have shown that temperature of transition is practically independent of polymer molecular weight, we have not considered the study of other molecular weights.

System [Copoly(PIPAM/VS) + H_2O]

Most of the copolymers of PIPAM studied so far [1] have been of the hydrophobically-modified type, which leads to a decrease of the LCST temperature. A similar effect is obtained when a hydrophylic compound is added to the solution [4] – (competition between the compound and the polymer for dissolution) -, but the opposite should be observed (rise of the LCS temperature) if that compound is incorporated in the polymer chain. Therefore, if one seeks to use PIPAM copolymers as switches working at about human body temperature, it becomes necessary to incorporate biologically compatible compounds in the polymer chain in order to obtain slightly higher LCS temperatures.

In Figure 3, plots of cloud-point temperatures of several copolymers of PIPAM (Table 1) with a vinyl saccharide monomer, copoly(N-isopropylacrylamide / 1-deoxy-1-methacrylamide-D-glucitol), are represented. For purposes of comparison, PIPAM is also shown.
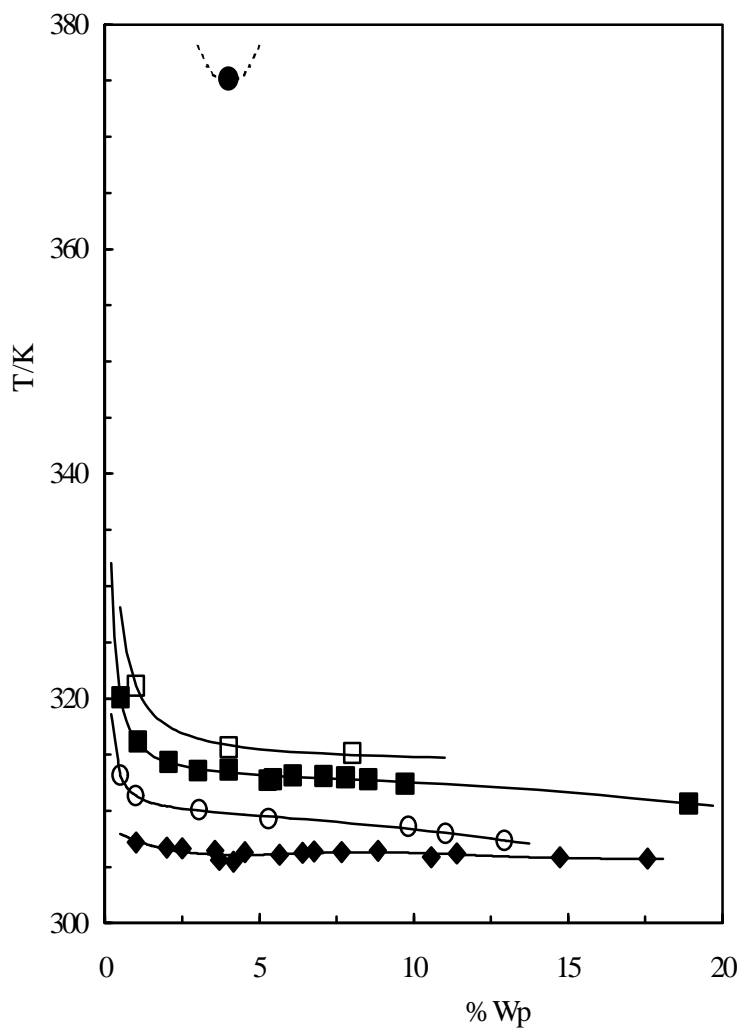
Figure 3: Comparison between LCST´s of PIPAM and copolymers in H_2O at a nominal pressure of 0.1 Mpa. (◆) P1, (○) CP1, (■) CP2, (□) CP3, (●) CP4 – see Table 1.

The most striking feature is the abrupt increase in LCST observed for the lowest molecular weight copolymer (CP4 – Table 1). This point was double-checked several times using fresh solutions of about 4.0 copolymer weight percent each time. This observation, *persi*, indicates the proximity of a hypercritical point [8-12] (or double critical temperature point).

This conclusion is corroborated by two other observations: (a) only in the close vicinity (3-5%) of this concentration is a transition observed – for higher and lower values a clear homogeneous one phase is always obtained up to 440 K; (b) deuterium substitution has a drastic effect on the LCST (see below). In other simpler words, the 13-14 mol percent copolymer of VS in PIPAM becomes completely soluble in H_2O, independently of temperature, for a weight average molecular weight smaller than 50,000 a.m.u.. In contrast with PIPAM [1,3], the copolymer LCST is molecular weight sensitive, becoming extremely molecular weight dependent at low M_W values.

Pressure effects have been investigated for two of the copolymers (CP1 and CP3) and are represented in Figure 4.
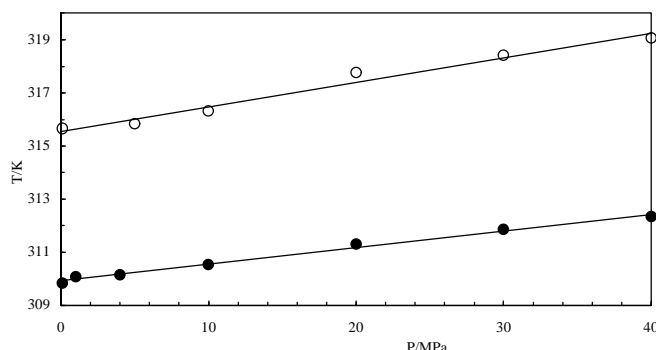

Figure 4: Pressure effects on the cloud-point temperature of nominal 4 % solutions of copoly (PIPAM/VS+H_2O). (●) CP1, (○) CP3. Straight lines represent least-square fits to a first order polynomial.

Results are qualitatively similar to those observed with PIPAM (Figure 2). Present technical difficulties in using the high pressure cell at high temperatures in a silicon oil bath prevented us from obtaining results for CP4 at distinct pressures, which we plan to do in the near future. Contrary to the plotted curves (Figure 4), pressure effects on LCST ought to be

very significant here, and this should be explored in detail. As expected, a comparison of the two represented curves shows a slight increase in slope as molecular weight decreases. At temperature hypercritical conditions, the theoretical value for dT_c/dp of the transition is infinity [10].

We have also studied the effect of physical addition of the vinylsaccharide to the solution of (PIPAM+water). A mixture of PIPAM (83 w. %) and VS (17 w. %) of overall composition of 4.6 w. % in water was prepared. As expected, the visual observation of cloud-point temperature dropped to 301.0±0.1 K, as compares with identically concentrated solutions of PIPAM+water (305.50±0.01 K) and (CP1)+water (310.11±0.01 K).

Isotope Effects

Deuterium substitution in the solvent (D_2O) for both 4 w. % solutions of PIPAM and all copoly (PIPAM/VS) has shown a very small effect of c.a. 1.0-1.2 ºC increase in the LCST compared to H_2O with the single exception of the very low molecular weight copolymer (CP4). Here, as expected, the effect is drastic and we have observed a decrease of 56 ºC (T_{LCST} = 319.05 K). In the case of PIPAM, Schild [1] has also reported (citing unpublished work) an elevation of 1.0±0.1 ºC for the LCST of aqueous PIPAM in 90% D_2O. Figure 5 shows the combined molecular weight and isotope effects for all copolymers, where, in the case of H_2O, we have assumed the Imre-Van Hook representation [13] of data. These authors developed a mean-field scaling relation (equation 1) where the expansion is done around an assumed hypercritical point, defined by T_c^* and X^* ($X^* = M_w^{*-1/2}$). M_w^* is the polymer molecular weight which locates the hypercritical point.

$$\left| \frac{T_c - T_c^*}{T_c^*} \right| = A \left| \frac{X - X^*}{X^*} \right|^a \tag{1}$$

$$X = M_w^{-1/2} \quad \text{for} \quad M_w^{-1/2} > 0$$

This leads to the prediction of a temperature hypercritical point and, thus, to the existence of a UCST branch at high temperatures. The speculation is that the phase diagram of the copolymers+water is inherently of the closed-loop type, though only the low temperature LCST branch is experimentally accessible. In accord with the predictions shown in Figure 5, (CP4+H_2O) was warmed up to 440 K with no observation of any reappearing homogeneous phase. One would have to go to much higher temperatures, but, there, thermal degradation of the copolymer would be inevitable.

Whether D_2O also shows a temperature hypercritical point, it remains an open question, which only can be solved by performing measurements with copolymers of $M_W <$ 50,000.
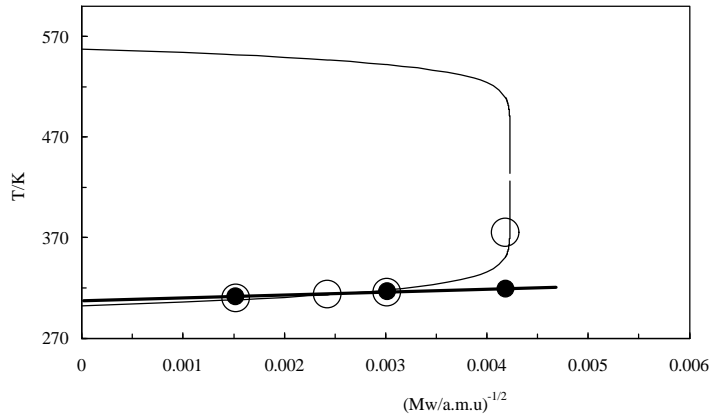

Figure 5: Temperature of transition *vs*. $(1/M_W)^{1/2}$ for copolymers at 4 w. % solutions in D_2O (●) and in H_2O (○) and at a nominal pressure of 0.1 MPa. Thick line is a first order least-squares fit to the deuterated solution. Thin line represents Equation 1 for the hydrogenated solution fitted at a reference hypercritical point of (T*=430 K; M_W*=0.559 x 10^5). The two-phase region is inside the envelope.

A final note of caution must be included. Both PIPAM and its copolymers have potential isotopic exchangeable hydrogens. These are those bonded to nitrogen (PIPAM and copolymers) and oxygen (copolymers). In the case of 4 % w. solutions, we have estimated that the number (moles) of potentially exchangeable H (in –OH groups) in copolymers per mol of D_2O is about 4×10^{-3}. This ratio shifts a probable isotopic exchange reaction towards the formation of a partially deuterated (D/H = 6/11) copolymer, maintaining the solvent at roughly the original content of deuterium. Similar conclusions are reached for PIPAM (in –NH groups) where that ratio is about 7×10^{-3} with the formation of a partially deuterated (D/H = 1/10) polymer. Thus, assuming that the isotopic exchange reaction is not kinetically controlled, one is in fact studying systems of partially deuterated polymers in a deuterated solvent. This remark does not affect the previous conclusions though. In the case of copolymers the analysis becomes additionally complicated by the possibility of formation of multiple *intra*molecular hydrogen bonds.

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